



a test agent, and (ii) ascertaining the presence, and more preferably the level, of onset or degree of severity of an inflammatory bowel disease or disorder, and comparing that with an untreated transgenic animal or transgenic animal treated with a control agent.

#### X. Exemplification

The following Table 1 teaches genes whose up-regulation or down-regulation, as indicated by "↑" and "↓", respectively, has been found to be associated with UC and CD. The genes are grouped according to their general functionality, as follows,

- I Chemokines + cytokines and growth factors
- II Inflammatory mediators
- III Cell cycle regulators/ transcription factors
- IV Cancer Related
- V HLA or immune function genes
- VI Antimicrobial
- VII ECM and remodelling
- VIII Others: Carbohydrate metabolism, Fatty acid metabolism, Protein folding/modification/degradation

Table 1

	UC	CD	Acc No.	Gene Names	Chromosome	Microsatellite Markers
I	↑21.4	↑12.8	Y00787	MDNCF/IL-8	4q13-q21	D4S392-D4S2947
I	↑15.3		X54489	MGSA (GRO1)	4q21	D4S400-D4S1534
I	↑7.9		M57731	MIP-2 (GRO2)	4q21	D4S392-D4S2947
I	↑8.9	↑4.1	M28130	IL8	4q13-q21	D4S392-D4S2947
I	↑6.8	↑3.9	X57351	IP-10	11	pTEL-D11S1318
I	↑6		J04130	MIP-1 /SCYA4	17q21	D17S933-D17S800
I	↑3.4		X53800	MIP-2 (GRO3)	4q21	D4S400-D4S1534
I	↑3.2		M69203	MIP-1 /SCYA2	17q21	D17S933-D17S800

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	UC	CD	Acc No.	Gene Names	Chromosome	Microsatellite Markers
I	↑4.6		X04500	pro-IL-1	2q14	D2S293-D2S121
I	↑3.5		X53296	IL-1RA	2q14	D2S293-D2S121
I	↑3.3		X04602	IL-6	7q21	D7S829-D7S673
I	↑3		J03756	Growth hormone 2 (GH2)	17q22-q24	D17S794-D17S795
I	↓3.5		D16431	Hepatoma-derived growth factor (HDGF)	17q2-q24	D17S794-D17S795
I		↓4	M58286	TNF Receptor member 1A	12p13.2	D12S99-D12S358
II	↑35.5		S75256	Neutrophil lipocalin (HNL)	-	-
II	↑10.4		X99133	Neutrophil gelatinase-associated lipocalin (NGAL)	9q34	D9S1821-D9S159
II	↑8.7		X85781	Nitric oxide synthase (NOS2)		-
II	↑5.1		X65965	Mitochondrial superoxide dismutase (SOD2)	6q25.3	D6S442-D6S1581
II	↑5.5	↑4.6	M22430	Phospholipase A2, group IIA (PLA2G2A)	1p35	-
II	↑5.3		X51441	Serum amyloid A (SAA)	11p	-
II	↑3.9		J03474	Serum amyloid A (SAA1)	11p15.1	D11S921-D11S1369
II	↑3.7		M21119	Lysozyme	-	-
II	↑3.4		D00408	Cytochrome P450 IIIA, polypeptide 7 (CPY3A7)	7	D7S479-D7S2545
II	↓4.2		D14662	Anti-oxidant protein 2	1	D1S2790-D1S2640
II	↓4.4		X64177	Metallothionein	-	-
II	↓8		J03910	Metallothionein-1G (MT1G)	16q13	D16S3057-D16S514
II	↑9		X85771	Nitric oxide synthase 2	10	D10S1786-D10S541
III	↑155	↑17.8	L08010	Regenerating islet-derived 1 (REG1B)	2p12	D2S286-D2S169
III	↑75	↑36.4	J05412	Regenerating islet-derived 1 (REG1A)	2p12	D2S139-D2S289
III	↑9.7	↑10.2	L15533	Pancreatitis-associated protein (PAP)	2p12	D2S169-D2S139
III	↑58.8		HG3566-HT3769	Zinc Finger Proteins	-	-
III	↑55.1	↑12.5	M87789	Ig 3 (IGHG3)	14q32.33	D14S65-qTEL
III	↑17.5	↑4.7	M26311	S100A9/calgranulin B	1q12-q22	D1S514-D1S2635
III	↑10.8	↑3.6	U08021	Nicotinamide N-methyltransferase (NNMT)	11q23.1	D11S1347-D11S939

	UC	CD	Acc No.	Gene Names	Chromosome	Microsatellite Markers
V	↓4.2	↓3.4	M13755	Inteferon stimulated protein 15-kDa (ISG15)	1	D1S243-D1S468
V		↓3.4	D11086	IL-2 receptor chain (IL2RG)	Xq13.1	DXS983-DXS995
V	↓3	↓6	M84526	Complement factor D (DF)	-	pTEL-D19S413
V	↓3.9		M38690	CD9 antigen	12p13	D12S99-D12S358
V	↑5		M28590	MHC Dg	6	
VI	↑20.4	↑40.8	M97925	Defensin 5 (DEFA5)	8pter-p21	D8S552-D8S549
VI	↑6.8	↑7.7	U33317	Defensin 6 (DEFA6)	8pter-p21	D8S277-D8S550
VII	↑16.2	↑3.3	L23808	MMP-12 (Macrophage elastase)	11q22.2-q22.3	D11S1339-D11S1343
VII	↑6.4		J05070	MMP-9 (Gelatinase B)	20q11.2-q13.1	D20S119-D20S197
VII	↑4.7		X54925	MMP-1 (Interstitial collagenase)	11q22.3	D11S1339-D11S1343
VII	↑4.2		X05232	MMP-3 (Stromelysin 1)	11q22.3	D11S1339-D11S1343
VII	↑13.3	↑3.8	L10343	Elastase specific inhibitor (Elafin)	20q12-q13	D20S119-D20S197
VII	↑11	↑3.1	Z74616	COL1A2	2q37	D2S2158-D2S125
VII	↑7.3		X52022	COL6A3	2q37	D2S2158-D2S125
VII	↑6.9	↑3.6	M55998	COL1A1	17q21.3-q22	D17S791-D17S794
VII	↑4.8		X06700	COL3A1	2q31	D2S2257-D2S115
VII	↑4.7		X15882	COL6A2	21q22.3	-
VII	↑3.9		X05610	COL4A2	13q34	D13S285-qTEL
VII	↑3.7	↑3.3	HG2157-HT2227	Mucin 4 (MUC4)	3q29	-
VII	↑3.1		X52003	Trefoil factor 1 (TFF1)	21q22.3	D21S1259-qTEL
VII		↑4.6	M22406	Intestinal mucin	-	-
VII	↑6.4		J03040	Osteonectin (SPARC)	5q31.3-q32	D5S436-D5S470
VII	↑4	↑3.2	X17042	Proteoglycan 1 (PRG1)	10q22.1	D10S210-D10S537
VII	↑3.9		D11428	Peripheral myelin protein 22 (PMP22)	17p12-p11.2	D17S804-D17S799
VII	↑3.8		X02761	Fibronectin 1 (FN1)	2q34	D2S137-D2S164
VII	↑3.7		M77349	Transforming growth factor beta-induced (TGF I)	5q31	D5S393-D5S500
VII	↑3.2		D13666	Osteoblast specific factor 2 (OSF-2)	13	D13S267-D13S1253
VII	↑3.1		M10321	von Willebrand	12p13.3	D12S99-D12S358

	UC	CD	Acc No.	Gene Names	Chromosome	Microsatellite Markers
				factor		
VII	↑3		L09190	Trichohyalin (THH)	1q21-q23	D1S439-D1S459
VII		↑3.1	D88422	Cystatin A (CSTA)	3q21	-
VII		↑4.7	X58199	Adducin 2 (ADD2)	2p13-p14	-
VII		↑3.7	M86933	Amelogenin (AMELY)	Yp11.2	-
VII		↓3.2	D45370	Adipose specific collagen-like 2 (APM2)	10	D10S1786-D10S541
VII		↓3.8	X73501	Cytokeratin 20	-	-
VII	↓4		U60061	Zygin 2	2	D2S367-D2S2230;D2S177-D2S119
VII		↓3	AF006087	Actin-related complex	3	D3S3591-D3S1283
VII		↓6	D87460	Paralemmin	19p13.3	pTEL-D19S413
VIII	↑50.5		D28416	Esterase D (ESD)	13q14.1-q14.2	D13S328-D13S168
VIII	↑4.7		M15656	Aldolase B	9q21.3-q22.2	D15S202-D15S157
VIII		↑6.3	J04040	Glucagon (GCG)	2q36-q37	D2S156-D2S376
VIII		↓4.4	L31801	Monocarboxylate transporter 1 (MCT1)	1p13.2-p12	D1S418-D1S514
VIII	↓3		D10523	Oxoglutarate dehydrogenase (OGDH)	7p14-p13	D7S521-D7S478
VIII	↓4		M12963	Alcohol dehydrogenase 1a (ADH1)	4q21-q23	-
VIII	↓4.5		Y00339	Carbonic anhydrase II (CA2)	8q22	D8S275-D8S273
VIII	↓4.9	↓3.1	L10955	Carbonic anhydrase IV (CA4)	17q23	-
VIII	↓12.7	↓3.1	L05144	Phosphoenolpyruvate carboxykinase 1, soluble (PCK1)	20q13.31	D20S183-D20S173
VIII	↑3		U07158	Syntaxin 4A (STX4A)	-	-
VIII		↑3	L27706	Chaperonin subunit 6A (CCT6A)	7	D7S530-D7S509
VIII	↓7	↓3.1	J04093	UDP-glycosyl-transferase 1 (UGT1)	2	D2S2158-D2S125
VIII	↓3.2		U20499	Sulfotransferase family 1A (SULT1A3)	16p11.2	-
VIII	↓3		M15182	-glucuronidase (GUSB)	7q21.11	-
VIII	↓4		U08854	UDP glucuronosyltransferase precursor (UGT2B15)	4q13	D4S1619-D4S392

	UC	CD	Acc No.	Gene Names	Chromosome	Microsatellite Markers
VIII	↓5		D87292	Thiosulfate sulfurtransferase (TST)	22	D22S277-D22S283
VIII	↓13	↓4	M22324	Aminopeptidase N/CD13 (ANPEP)	15q25-q26	D15S202-D15S157
VIII	↓12	↓7	M22960	Protective protein for b-galactosidase (PPGB)	20q13.1	D20S119-D20S197
VIII	↑3.4		X90908	Fatty acid binding protein 6 (FABP6)	5q23-q35	-
VIII		↑4.1	J02874	Fatty acid binding protein 4 (FABP4)	8q21	-
VIII	↓3		M10050	Fatty acid binding protein 1 (FABP1)	11p15.5	D11S1318-D11S909
VIII	↓3		L24774	Mitochondrial d3, d2-CoA-isomerase	-	
VIII	↓4		D16294	Mitochondrial 3-oxoacyl-CoA thiolase (ACAA2)	18	D18S1118-D18S474
VIII	↓4		M77144	3 b-hydroxysteroid dehydrogenase (HSD3B2)	1p13.1	D1S418-D1S514
VIII	↓5		D10511	Mitochondrial acetoacetyl-CoA thiolase	-	-
VIII	↓7		Z80345	Acyl-Coenzyme A dehydrogenase (ACADS)	12q22-qter	D12S366-D12S340
VIII	↓7		L11708	17 b-hydroxysteroid dehydrogenase II (HSD17B2)	16q24.1-q24.2	D16S515-D16S422
VIII	↓7		U26726	11 b-hydroxysteroid dehydrogenase II (HSD11B2)	16q22	D16S3031-D16S3139
VIII	↓3.5		X93036	MAT8 protein	19	D19S425-D19S418
VIII	↓12.2	↓4	M97496	Guanylate cyclase activator 1B (UCA1B)	6p21.1	D1S2843-D1S417
VIII		↑4.2	D17400	6-pyruvoyl-tetrahydropterin synthase (PCBD)	10q22	D10S210-D10S537
VIII		↑3.3	D21262	KIAA0035	-	-
VIII		↑3.1	AB002365	KIAA0367	-	-
VIII		↓4.5	M11119	Endogenous retrovirus envelope region	-	-
VIII	↓3.1		M19961	Mitochondrial cytochrome c oxidase Vb (COX5B)	2cen-q13	D2S113-D2S176